

IN THE CLAIMS

1. (Currently amended) A particulate composition for delivery to the pulmonary system comprising:

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particles comprising a saturated, zwitterionic phospholipid and a polyvalent cation ~~in an amount at a molar ratio of polyvalent cation to phospholipid of at least 0.05~~ effective to increase the gel-to-liquid crystal transition temperature of the particle compared to particles without the polyvalent cation, wherein the particulate composition is storage stable.

2. (Original) A particulate composition according to claim 1 wherein said gel-to-liquid crystal transition temperature is greater than the storage temperature for said composition by at least 20°C.

3. (Original) A particulate composition according to claim 2 wherein said gel-to-liquid crystal transition temperature is greater than the storage temperature for said composition by at least 40°C.

4. (Original) A particulate composition according to claim 1 further comprising a surfactant selected from the group consisting of nonionic detergents, nonionic block copolymers, ionic surfactants and combinations thereof.

5. (Original) A particulate composition according to claim 4 wherein the surfactant is selected from the group consisting of sorbitan esters, ethoxylated sorbitan esters, fatty acids, salts, sugar esters, ethylene oxides, and combinations thereof.

6-7 (Cancelled)

8. (Original) A particulate composition according to claim 1 wherein the polyvalent cation is a divalent cation.

9. (Original) A particulate composition according to claim 8 wherein the divalent cation is selected from the group consisting of calcium, magnesium, or zinc.

10. (Cancelled)

11. (Currently amended) A particulate composition according to claim 8 ~~40~~ wherein the molar ratio of divalent cation to phospholipid is 0.05 – 2.0.

12. (Currently amended) A particulate composition according to claim 8 ~~40~~ wherein the molar ratio of divalent cation to phospholipid is 0.25 – 1.0.

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13. (Original) A particulate composition according to claim 12 wherein the divalent cation is calcium.

14. (Previously amended) A particulate composition according to claim 13 wherein the molar ratio of calcium to phospholipid is about 0.50.

15. (Original) A particulate composition according to claim 1 wherein the phospholipid comprises a natural or synthetic lung surfactant.

16. (Previously amended) A particulate composition according to claim 1 further comprising an active agent.

17. (Previously amended) A particulate composition according to claim 16 wherein the active agent is selected from the group consisting of nicotine, human growth hormone, parathyroid hormone, leuprolide, budesonide, tobramycin, albuterol, insulin, interferon alpha, interferon beta, amphotericin, fluticasone, salmeterol, formoterol, and salts thereof.

18. (Original) A particulate composition according to claim 1 further comprising a polymer selected from the group consisting of polysaccharides, polyvinyl alcohol, polyvinyl pyrrolidone, polylactides, polyglycolides, polyethylene glycol, or mixtures thereof.

19. (Original) A particulate composition according to claim 1 comprising particles having a mass median diameter of less than 20 microns.

20. (Original) A particulate composition according to claim 19 wherein the mass median diameter is within 0.5 – 5 microns.

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21. (Original) A particulate composition according to claim 19 wherein the particles comprise an aerodynamic diameter of less than 10 microns.
22. (Original) A particulate composition according to claim 21 wherein the aerodynamic diameter is within 0.5 – 5 microns.
23. (Original) A particulate composition according to claim 1 comprising an emitted dose of at least 40%.
24. (Original) A particulate composition according to claim 1 comprising an emitted dose of at least 60%.
25. (Original) A particulate composition according to claim 1 comprising an emitted dose of at least 90%.
26. (Original) A particulate composition according to claim 1 further comprising a non-aqueous suspension medium.
27. (Original) A particulate composition according to claim 1 further comprising an excipient selected from the group consisting of amino acids, carbohydrates, inorganic salts, organic salts, carboxylic acids, and mixtures thereof.
28. (Original) A particulate composition according to claim 27 wherein the excipient is selected from the group consisting of hydrophobic amino acids, monosaccharides, disaccharides, polysaccharides, sodium citrate, citric acid, ammonium carbonate, ammonium acetate, and ammonium chloride.
29. (Original) A particulate composition according to claim 1 further comprising a density of less than 0.5 g/cm³.
30. (Original) A particulate composition according to claim 29 wherein the density is less than 0.05 g/cm³

31. (Currently amended) A particulate composition comprising biodegradable particles comprising a zwitterionic phospholipid and a polyvalent cation at a molar ratio of polyvalent cation to phospholipid of at least 0.05 wherein the composition comprises a gel-to-liquid transition temperature Tm and a storage temperature Ts wherein Tm > Ts by at least 20 °C.

32. (Currently amended) A particulate composition for delivery to the pulmonary system comprising:

20 – 99.9% of a saturated, zwitterionic phospholipid;
a polyvalent cation in an amount at a molar ratio of polyvalent cation to phospholipid of at least 0.05 effective to increase the gel-to-liquid crystal transition temperature of the particle compared to particles without the polyvalent cation; and, optionally
0.1 – 80% active agent;
wherein the composition is in the form of hollow and porous particles.

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33-42 (Cancelled)

43. (Misnumbered)

44. (Currently amended) A method for delivery to the pulmonary system comprising administering to the respiratory tract of a patient in need of treatment an effective amount of storage stable particles comprising a saturated, zwitterionic phospholipid and a polyvalent cation present at a molar ratio of polyvalent cation to phospholipid of at least 0.05 in an amount effective to increase the gel-to-liquid crystal transition temperature of the particle compared to particles without the polyvalent cation.

45. (Original) A method according to claim 44 wherein the particulate composition comprises particles having a mass median diameter of less than 20 microns.

46. (Original) A method according to claim 45 wherein the mass median diameter is within 0.5 – 5 microns.

47. (Original) A method according to claim 45 wherein the particles comprise an aerodynamic diameter of less than 10 microns.

48. (Original) A method according to claim 47 wherein the aerodynamic diameter is within 0.5 – 5 microns.

49. (Original) A method according to claim 44 wherein the particles comprise polyvalent cation at a molar ratio of cation:phospholipid of 0.25-1.0

50. (Original) A method according to claim 49 wherein the polyvalent cation comprises calcium.

51. (Original) A method according to claim 48 wherein the particles comprise a density of less than 0.5 g/cm³.

52. (Original) A method according to claim 51 wherein the particles further comprise an active agent selected from the group consisting of nicotine, human growth hormone, parathyroid hormone, leuprolide, budesonide, tobramycin, albuterol, insulin, interferon alpha, interferon beta, amphotericin, fluticasone, salmeterol, formoterol, and salts thereof.

53. (Previously added) A particulate composition according to claim 1 wherein the particles are hollow and porous.

54. (Previously added) A particulate composition according to claim 16 comprising 0.1 – 80% w/w of an active agent.

55. (Previously added) A particulate composition according to claim 31 wherein the particles are hollow and porous.

56. (Previously added) A particulate composition according to claim 31 wherein the storage temperature is approximately room temperature.

57. (Previously added) A particulate composition according to claim 56 wherein the T_m > T_s by at least 40 °C.

58. (Previously added) A particulate composition according to claim 56 wherein the phospholipid is selected from dipalmitoylphosphatidylcholine or distearoylphosphatidylcholine.

59. (Currently amended) A particulate composition comprising a structural matrix comprising a saturated, zwitterionic phospholipid and a polyvalent cation ~~in an amount at a molar ratio of polyvalent cation to phospholipid of at least 0.05~~ effective to increase the gel-to-liquid crystal transition temperature of the particle compared to particles without the polyvalent cation, wherein the composition is storage stable.

60. (Previously added) A particulate composition according to claim 59 wherein the phospholipid comprises dipalmitoylphosphatidylcholine or distearoylphosphatidylcholine.

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61. (Previously added) A particulate composition according to claim 59 wherein the polyvalent cation is a divalent cation.

63. (Cancelled)

64. (Currently amended) A particulate composition according to claim 59 63 wherein the molar ratio of divalent cation to phospholipid is 0.05 – 2.0.

65. (Currently amended) A particulate composition according to claim 59 63 wherein the molar ratio of divalent cation to phospholipid is 0.25 – 1.0.

66. (Previously added) A particulate composition according to claim 59 further comprising an active agent.

67. (Previously added) A particulate composition according to claim 66 wherein the active agent is selected from the group consisting of nicotine, human growth hormone, parathyroid hormone, leuprolide, budesonide, tobramycin, albuterol, insulin, interferon alpha, interferon beta, amphotericin, fluticasone, salmeterol, formoterol, and salts thereof.

68. (Previously added) A particulate composition according to claim 61 wherein the divalent cation is calcium.

69. (Previously added) A particulate composition according to claim 68 wherein the molar ratio of calcium to phospholipid is about 0.50.

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70. (Previously added) A particulate composition according to claim 59 wherein the composition comprises a gel-to-liquid crystal transition temperature T_m and a storage temperature T_s wherein $T_m > T_s$ by at least 20 °C.

71. (Previously added) A particulate composition according to claim 70 wherein $T_m > T_s$ by at least 40 °C.